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09/955,663	09/19/2001	David M. Roche	19629-7006	1221

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EXAMINER

MORAN, MARJORIE A

ART UNIT PAPER NUMBER

1631

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/955,663

Applicant(s)

ROCKE ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-12 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims recite a series of mathematical steps, equivalent to a mental process.

Applicant is reminded that a mental process is not statutory subject matter, as set forth below.

MPEP 2106.IV.B.1

If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. *Schrader*, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

MPEP 2106.IV.B.2 (b) ii

A process that merely manipulates an abstract idea or performs a purely mathematical algorithm is nonstatutory despite the fact that it might inherently have some usefulness. In *Sarkar*, 588 F.2d at 1335, 200 USPQ at 139, the court explained why this approach must be followed: No mathematical equation can be used, as a practical matter, without establishing and substituting values for the variables expressed therein. Substitution of values dictated by the formula has thus been viewed as a form of mathematical step. If the steps of gathering and substituting values were alone sufficient, every mathematical equation, formula, or algorithm having any practical use would be per se subject to patenting as a "process" under 101. Consideration of whether the substitution of specific values is enough to convert the disembodied ideas present in the formula into an embodiment of those ideas, or into an application of the formula, is foreclosed by the current state of the law. For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See *Alappat*, 33 F.3d at 1543, 31 USPQ2d at 1556- 57 (quoting *Diamond v. Diehr*, 450 U.S. at 192, 209 USPQ at 10). See also *Alappat* at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) ("unpatentability of the principle does not defeat patentability of its practical applications") (citing *O'Reilly v. Morse*, 56 U.S. (15 How.) at 114-19). A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible and

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useful result; i.e., the method recites a step or act of producing something that is concrete, tangible and useful. See AT&T, 172 F.3d at 1358, 50 USPQ2d at 1452.

MPEP 2106.II.A

The claimed invention as a whole must accomplish a practical application. That is, it must produce a "useful, concrete and tangible result." *State Street*, 149 F.3d at 1373, 47 USPQ2d at 1601-02. The purpose of this requirement is to limit patent protection to inventions that possess a certain level of "real world" value, as opposed to subject matter that represents nothing more than an idea or concept, or is simply a starting point for future investigation or research (*Brenner v. Manson*, 383 U.S. 519, 528-36, 148 USPQ 689, 693-96); *In re Ziegler*, 992, F.2d 1197, 1200-03, 26 USPQ2d 1600, 1603-06 (Fed. Cir. 1993)).

The claimed method does not recite any physical method step or transformation of data which may render it statutory. In the absence of one of these "safe harbors", a method MAY be statutory when it recites a concrete, tangible and useful result, as set forth above. However, none of the claims actually recites any particular result. The last step (g) of instant claim 2 is one of estimating the variance of a signal. It is unclear whether it is the variance or the signal itself which is intended to be the "result" of step (g). Further, no result is generated or output in a "concrete and tangible" form such that it could be comprehended and thus be "useful" to one performing the method. As the claimed method fails to recite either a "safe harbor" or a concrete, tangible and useful result, the claims do not recite statutory subject matter and is rejected.

Claims 2-12 are also rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The preamble to claim 2 recites a method for estimating the precision of measurements from a gene expression microarray. A method of estimating the precision, or accuracy, of gene expression array measurements MAY have utility.

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However, the claimed method steps do not result in an estimation of precision or accuracy of such measurements. The claimed steps of the method only result in estimating a variance of a measured signal which indicates the amount of a biological molecule. The specification does not set forth a specific and substantial utility for estimating the variance (changes) in measurements taken from a gene expression microarray, and no well established utility is provided for such a method in the prior art. As it is unclear whether the method, in fact, actually estimates a precision for measurements taken from a gene expression microarray, and no utility is set forth for the claimed method steps, the claims lack utility, and are rejected.

Claim Rejections - 35 USC § 112, 1st para.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a LACK OF WRITTEN DESCRIPTION rejection.

Claim 2, in step (f), recite measuring a signal, y, wherein the signal indicates an amount of a biological molecule, which is not supported by the instant specification.

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The specification, on page 2, discloses an equation similar to the second recited in step (g) of claim 2, wherein y is defined as the observed intensity measured (in an experimental assay). While an observed intensity (e.g. color) may be proportional to an "amount", the intensity itself is not the "amount" of molecule measured in the assay.

The specification discloses another equation on page 4, with similar variables to that of page 2, but discloses that " y " is the peak area of a measurement. Again, a peak area may be proportional in some manner to an "amount" of a molecule, but is not the amount itself. It is well known in the art that peak area and intensities are not necessarily directly proportional to concentrations, and that mathematical manipulation and/or comparison to standards is often necessary to convert a measured intensity or peak area into an "amount". The first line of page 5 defines " y " as a "response", in an Equation 3, which is identical to that of step (g) of claim 2. Thus, the specification provides a disclosure wherein y is either an intensity, a peak area, or a "response, any of which MAY be interpreted to be a "signal", but does NOT disclose that the intensity, peak area, or response is a specific "indication" or measurement of an amount of a biological molecule. Thus, the specification fails to provide a full and complete description of measurement of a signal " y ", which indicates an amount of a biological molecule.

Claims 2-12 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

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one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A method wherein μ is an "amount" is new matter. The originally filed claims did not define μ . The originally filed specification, on pages 2 and 4, defines μ as an expression level, in arbitrary units, in an equation (termed Equation 1 on page 4) identical to the second equation recited in step (g) of claim 2. Neither of these definitions of μ is supportive of an "amount". The specification, on page 5, defines μ as a "concentration"; however, an "amount" is a broader limitation than a concentration, therefore the disclosure on page 5 fails to provide support for the broader limitation added in amendment, therefore claim 2 recites new matter.

Claim Rejections - 35 USC § 112, 2nd para.

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. Rejections not reiterated below have been withdrawn in view of the amendment filed 7/8/05.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites a step of estimating a standard deviation of an additive error component, but does not recite whether the additive error component is somehow

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related to the measurements of step (a). It is unclear what the "error component" is intended to refer to; i.e. the low-level measurements of step (a), some other measurements, some constant or variable associated with a measuring device, etc. Further, it is unclear if the error component is one that is measured, and thus "taken from" the gene expression microarray of the preamble, or whether the error component is a previously provided value. For these reasons, claim 2 is indefinite.

Claim 2 recites estimating a background parameter, but does not recite what the background is related to, i.e. a "background" of color, fluorescence, luminescence, inherent background from a measuring apparatus, background due to salts or other buffer components, etc. As it is unclear whether the background parameter is one of the "measurements" taken from the gene expression microarray of the preamble, or is intended to be from some other source, claim 2 is indefinite.

Claim 2 recites the phrase "high-level" with regard to data measurements. The specification does not define the term "high-level" and one of skill in the art would not be apprised of the metes and bounds intended by applicant for data measurements which are "high-level". Claim 2 defines "low-level" data to be that below a cutoff value; however, it is not known whether "high-level" data is intended to be any data above a cutoff value, or whether the data is intended to be "higher" than some other level of data (e.g. mid-level), or is data wherein the values attain certain degree of complexity. For these reasons, claim 2 is indefinite.

Claim 2 recite two different equation in step (g) wherein terms are apparently defined differently be the specification, but not in the claims. The originally filed

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specification, on pages 2 and 4, defines μ as an expression level, in arbitrary units, in an equation (termed Equation 1 on page 4) identical to the second equation recited in step (g) of claim 2. The specification, on page 5, defines μ as a "concentration" in Equation 3, which is identical to the first equation of claim 2. However, claim 2 defines μ as an "amount", apparently for both equations. The discontinuity between the specification and claims renders it unclear what μ is actually intended to represent, therefore claim 2 is indefinite.

Claim 2 recites "use" of an algorithm to establish a cutoff, but does not recite what the "cutoff" is for or is related to; i.e. a signal level, a concentration, an amount of ligand bound, a level of hybridization, etc. As it is unclear what sort of cutoff is intended, claim 2 is indefinite.

Claim 2 recites series of steps, but fails to recite any connection between them. Only steps (d) and (e) appear to have any relationship. The relationship, if any between step (a) and any other method step, between step (b) and any other step, between step (c) and any other step is unclear. It is further unclear what relationship, if any, step (d) and (e) have with any other step. It is also unclear whether step (f) has relationship with any other step. It is not whether the measured signal "y" of step (f) is intended to be the same "y" as that in the equations of step (g), not what relationship, if any, is intended between steps (f) and (g) and any other step of the claim. Claim 2 is therefore incomplete for omitting essential elements, such omission amounting to a gap between the elements.

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Claims 3 and 4 recite the limitation "the initial set", each in step (b). There is insufficient antecedent basis for this limitation in the claims. Further, it is unclear what the "initial set" is intended to comprise; i.e. measurements, data points, amounts, concentrations, etc., therefore the phrase renders the claims indefinite.

Claims 3 and 4 recite repeating steps "until an algorithm converges." It is unclear what limitation is intended by this phrase, and what the algorithm is intended to converge TO; i.e. a consensus, a minimum, a maximum, an average, etc., therefore the claims are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of ROCKE et al. (Technometrics (May, 1995) vol. 37, no. 2, pages 176-184) and PABON et al. (Int'l. Genome Sequencing and Analysis Conf. (Sep. 12-15, 2000), vol. 12, p. 82).

PABON teaches a method of gene expression analysis using DNA, specifically cDNA and various RNA's, including mRNA. PABON teaches analysis of a coefficient of variance (CV) to show accuracy in his method. PABON does not teach the specific mathematical steps of the instant claims for his statistical analysis.

ROCKE teaches a method for estimating the precision or accuracy of measurements for any analytical chemistry-type of assays which includes an analysis of coefficient of variance (p. 176 and 182). ROCKE teaches the same steps and equations as set forth in the instant claims (pages 177-178), and teaches that his method may be used in a wide variety of situations (p. 182: Conclusion).

It would have been obvious to one of ordinary skill in the art at the time of invention to have used the statistical analysis of ROCKE to determine a CV in order to estimate accuracy in the method of PABON where the motivation would have been to use an improved method for measuring error across a full concentration range, as taught by ROCKE (abstract, p. 176).

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
9/29/05